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NEMSK.P-038
PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Rosen et al.
Serial No.: 09/937,192
Filing Date: 9/21/01
For : Methods and Compositions for Degradation and/or Inhibition of HER-
Family Tyrosine Kinases

Examiner: B. Kifle
Group Art Unit: 1624

FAX RECEIVED**AUG 28 2003****GROUP 1600**RESPONSE TO FINAL REJECTION

This is in response to the Official Action mailed June 11, 2003 for the above-captioned application.

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Reconsideration of the application in view of the remarks herein is respectfully requested.

The Examiner rejected claims 3, 4, 6 and 9-34 under 35 USC § 112, second paragraph. The Examiner asserts that the claims are indefinite because "the scope of the ansamycin antibiotic is unclear," and criticizes the Applicants' prior definition. Applicants point out that the information they have provided to the Examiner conforms to the definitions and the usage in the art. The term "anasmycin antibiotic" is used in patents and in the literature to describe compounds such as geldanamycin, herbimycin A (both of which are mentioned on page on Page 1 line 26 and Page 4, line 13 of the application). The fact that it is used without explication refutes the Examiner's position that the artisan does not understand the meaning of the term. Applicants further enclose two additional publications, US Patent No. 3,954,737 and K. Rinehart, *Accounts of Chem. Res.* 5: 57-64 (1972), both of which expressly state the same definition previously provided by Applicants.

Applicants further note that the Examiner's unsupported contention that the definition must be wrong because the term "aliphatic" does not encompass nitrogen containing

I hereby certify that this paper and any attachments named herein are transmitted to the United States Patent and Trademark Office, Fax number: 703-872-9307 on August 27, 2003.

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August 27, 2003
Date of Signature

MSK.P-038
PATENT APPLICATION

groups is not only inconsistent with the usage in the art relating to ansamycins, it is inconsistent with the ordinary meaning of the term in the chemical arts generally. Specifically, one online glossary defines "aliphatic" as "An organic compound that does not contain ring structures." <http://antoine.frostburg.edu/chem/senese/101/glossary/a.shtml#aliphatic>. Another defines it as "pertaining to any member of one of the major groups of organic compounds, those having a straight or branched chain structure." http://www.mercksource.com/pp/us/cns/cns_hl_dorlands.jspzQzpgzEzzSzppdocszSzuszSzcommonzSzdorlandzSzdorlandzSzdmd_a_24zPzhtm#918702. Yet another defines it as "of, relating to, or being an organic compound having an open-chain structure (as an alkane)." <http://www.m-w.com/cgi-bin/dictionary?book=Dictionary&va=aliphatic>. In none of these definitions is there any limitation that would exclude nitrogen or other non-carbon atoms. Furthermore, the aromatic nucleus is aromatic prior to the attachment of the bridge. Thus, it is not relevant whether or not the quinone is aromatic after this attachment.

The Examiner also asserts without explanation or support that the quinone is not aromatic. Again, this argument is inconsistent with the usage in the art as exemplified by Rinehart and other documents of record. Furthermore, dictionary definitions of "quinone" refer to it as an aromatic. For example, one online dictionary defines quinone as

Any of a class of aromatic compounds found widely in plants, especially the yellow crystalline form, $C_6H_4O_2$, used in making dyes, tanning hides, and photography.

<http://dictionary.reference.com/search?q=quinone>. Another states that:

This is a general name for aromatic compounds that have two atoms of hydrogen replaced by two atoms of oxygen, usually in the para position.

<http://www.drumlib.com/dn/qu.htm>. Accordingly, Applicants submit that the rejection under § 112, second paragraph should be withdrawn, because there is no reason to imagine that a person skilled in the art would have any difficulty determining the scope of the claims.

The Examiner has also rejected claims 12-30 as lacking enablement. The Examiner states that "undue experimentation is required to use compounds of the instant claims to treat

MSK.P-038
PATENT APPLICATION

cancers generally or those which over-express a HER-family kinase." Applicants point out that claim 12 is directed to a method for destruction of cells, not a method for treating cancer. Thus, the application of this rejection to claim 12 is not understood.

Applicants further inquire **why** the Examiner has maintained this rejection while refusing to comment on the references showing the diverse activity of geldanamycin and related species against many different types of cancer. It is inappropriate to force Applicants to proceed to appeal with an incomplete record in which the basis for the Examiner's apparent dismissal of the evidence of record is not even stated.

Finally Applicants respectfully disagree with the Examiner's characterization of *In re Brana* as having different facts. The Examiner says that this case is not controlling because (1) "the compounds on appeal were of much narrower scope"; (2) there were no method claims; (3) the compounds on appeal "were similar in structure to compounds displaying *in vivo* tumor activity." Applicants submit that these three distinctions are not supported by a consideration of the Brana case and the present application.

The assertion that the Brana compounds were of narrower scope has not been explained by the Examiner. The Brana compound has 4 variable substituents, each of which can be independently selected from a long list of possible combinations. There is no meaningful distinction between this claim and those of the present application in terms of the number of compounds, since the number in each case is large.

The comment that Brana is inapplicable because there were no method claims ignores that holding in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971) (which was cited in this case but not mentioned by the Examiner), where it is noted that:

a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112, *unless* there is a reason to doubt the objective truth of the statements contained therein, which must be relied upon for an enabling disclosure.

MSK.P-038
PATENT APPLICATION

It also ignores the evidence submitted upon which the Examiner has not commented. Furthermore, it seeks to apply a case for what it does not say, when the reason nothing was said was that the issue was not before the court. This is improper.

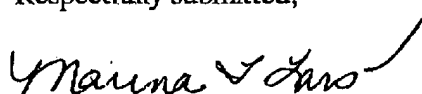
Here, the Examiner has not offered any reasoning as to why the assertions of general utility in this application, given the suggested mechanism of action, and the evidence of involvement of the targeted species in numerous different cancer types. As such, the Examiner has failed to meet the burden discussed in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971), where it is noted that:

a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112, *unless* there is a reason to doubt the objective truth of the statements contained therein, which must be relied upon for an enabling disclosure.

The Examiner should either withdraw the rejection or address the merits of Applicants' previously submitted arguments and evidence (Amendment filed 7/22/02, Exhibits A-H).

In view of the foregoing amendments and arguments, Applicants submit that all claims are in form for allowance. Favorable reconsideration and allowance of all claims are respectfully urged.

Respectfully submitted,



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